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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/404,706	09/23/1999	LEWIS T. WILLIAMS	2300-1492	8702

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EXAMINER	
ZHOU, SHUBO	
ART UNIT	**PAPER NUMBER**
1631	

DATE MAILED: 08/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/404,706	WILLIAMS ET AL.	
	Examiner	Art Unit	
	Shubo (Joe) Zhou	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 April 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *67,68,70,71,73 and 74* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *67-68, 70-71, and 73-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Petition

1. Applicants' petition, filed 4/20/04, for the Office to withdraw the Notice of Abandonment mailed 4/6/04 is received. The evidence provided by applicants supports that applicants did indeed timely file a response to the Office action mailed 7/16/03. Thus, the petition is granted and the Notice of Abandonment is hereby withdrawn.

M Neboldt
SPE AU 1631
8/19/04

Amendments

2. Applicant's amendments and request for reconsideration in the response, filed on 10/16/03, is acknowledged and the amendments entered.

Currently, claims 67-68, 70-71, and 73-74 are pending under consideration.

Applicant's arguments in response to the previous Office Action mailed 7/16/03, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous Office action are hereby withdrawn. The following rejections and/or objections are either reiterated from the previous Office action(s) or newly added, and constitute the complete set presently being applied to the instant application.

Claim Rejections-35 USC § 101/ § 112

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. The following is a quotation of the **first** paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 67-68, 70-71, and 73-74 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility due to its not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility.

This rejection is reiterated from the previous Office action and maintained for reasons of record.

Claims 67-68, 70-71, and 73-74 are drawn to nucleic acid molecules comprising the sequence of SEQ ID NO:635 or 100 contiguous nucleotides thereof, or vector comprising the nucleic acid molecules and recombinant cell comprising such vector. The claimed nucleic acids are not supported by a specific asserted utility because none of the disclosed uses of the nucleic acids in the specification is specific. For example, the specification states that the polynucleotides can be used in mapping, tissue profiling, detection of expression level, etc. (see pages 23-43). These are not specific uses for the claimed nucleic acids because they are generic to any nucleic acids derived from an organism. Applicants list a number of possible uses but fail to assert a specific utility for the claimed nucleic acids. None of the utilities asserted is specifically linked to the claimed nucleic acids comprising the sequence of SEQ ID NO:635 or portions thereof. Further, the claimed nucleic acids are not supported by a substantial utility because no substantial utility has been established for the claimed subject matter. For example, the specification states that the nucleic acids can be used for diagnosis of human disease by monitoring the expression level of the nucleic acids (page 27). However, the specification

does not provide specific diseases that can be diagnosed by monitoring the expression level of the claimed nucleic acids, nor does it provide whether hyper- or hypo-expression of the nucleic acids is associated with disease. Therefore, one of skill in the art would have to perform further research to determine what, if any, disease is specifically linked to the mis-regulation of the expression of the claimed nucleic acids, and what expression pattern of the claimed nucleic acids (e.g. hyper-expression or hypo-expression) is linked to the disease in order to find any practical usage for the nucleic acids. The apparent need for such further research indicates that the claimed nucleic acids are not disclosed as to a currently available or substantial utility.

Further, neither the specification as filed nor any art of record discloses or suggests any property or activity for the claimed nucleic acid such that a non-asserted utility would be well established for the nucleic acids.

It is noted that Table 2A on page 120 of the specification appears to assert that SEQ ID NO:635 shares homology with a database sequence M13973, which appears to encode a bovine protein kinase C. It is not clear from the specification as to the percentage of homology, but the search results by the Office of the database GenEmbl with SEQ ID NO:635 as query show that the overall match of SEQ ID NO:635 with M13973 is only 25.3%. See result No.84 of the attached search "Summaries". One of skilled in the art, however, would have reasons to doubt that the claimed nucleic acids indeed encode a protein kinase C protein for the following reasons:

Firstly, it would have been well known in the art that sequence similarity does not reliably correlate to sequence similarity and that sequence similarity does not reliably result in similar or identical biological activities. For example, it would have been well

known that even a single nucleotide or amino acid change or mutation is able to destroy the function of the biomolecule in many instances, albeit not in all cases. In the absence of factual evidence characterizing the structural and functional components of the biomolecule, the effects of these changes are largely unpredictable as to which ones will have a significant effect and which ones will be silent mutations having no effect. The prior art cannot *unambiguously* assign function to an unknown gene based on a homology comparison. The following example demonstrates that assignment of a metabolic gene to a known function based on homology comparisons alone provide improper functional assignment (see the homology-based methods of functional assignment of Everett et al., Nature Genetics *17*, 411-422, **1997** in light of the experimental conclusions of Scott et al., Nature Genetics *21*, 440-443, **1999**). Everett et al. disclose a homology-based functional assignment to a putative, mutated sulfate transporter gene (PDS; which encodes "pendrin") identified through positional cloning in Pendred syndrome populations. The homology-based searches were carried out using BLAST and PSI-BLAST with commercial databases using human pendrin as the query sequence. The conclusions of Everett et al. based upon the homology comparisons were that pendrin was a transporter of sulfate. However, experimental studies by Scott et al., clearly demonstrate that pendrin, which has: 1) 29% homology to the rat sulfate-ion transporter encoded by *Sat-1*; 2) 32% homology to the human diastrophic dysplasia sulfate transporter *DTD*; and 3) 45% homology to the human sulfate transporter down-regulated in adenoma encoded by *DRA*, is not a transporter of sulfate, but of chloride and iodine instead.

Secondly, as set forth above, the claimed invention is a genus that encompass a great variety of species which may have distinct different structures due to the recitation

of a fragment of 100 nucleotides of SEQ ID NO:635 or nucleic acids hybridizable thereto. One skilled in the art would have serious doubt that these different nucleic acids with different structures would encode protein kinase C.

Given the above and in light of the art recognized fact that minor sequence differences can significantly affect a protein's function, one of skilled in the art would have reasonable doubt that SEQ ID NO:635 does encode a protein kinase C, and would perform further research to reasonably confirm applicants' assertion.

Assuming *arguendo* that the polypeptide encoded by SEQ ID NO:635 were a member of the protein kinase C family, one of skilled in the art would still have to perform further research to determine what specific protein the so-called protein kinase C encoded by SEQ ID NO:635 interacts with and what specific function the protein kinase C has because it has been well known that the protein kinase C family comprises a variety of members with different biological functions including release and exocytosis, cell growth and morphogenesis. See Nishizuka, Y. (Abstract).

In conclusion, since there is a significant question as to whether the claimed nucleic acids encode protein kinase C, applicants could not rely upon a well-established utility for the claimed nucleic acids.

Applicant's arguments filed 10/16/03 have been fully considered but they are not persuasive.

Applicants argue that the specification assert that the claimed polynucleotides are useful in cancer diagnosis such as lung, breast, prostate cancers. Thus, the utility requirement of 35 USC 101 is satisfied. This is not persuasive.

In *Brenner v. Manson*, the Supreme Court of the U.S., 148 USPQ 689 (1966) held that:

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point – where specific benefit exists in currently available form – there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.
>
> These arguments for and against the patentability of a process which either has no known use or is useful only in the sense that it may be an object of scientific research would apply equally to the patenting of the product produced by the process.

In the instant case, while this asserted utility, i.e. diagnosis for lung cancer, etc., appears to be specific, it is not substantial because further research is needed to determine how the polynucleotides can be used in the cancer diagnosis. Thus, the claimed polynucleotides lack a currently available utility.

6. Claims 67-68, 70-71, and 73-74 are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention lacks a patentable utility due to its not being supported by a specific, substantial, and credible utility or, in the alternative, a well-established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

This rejection is reiterated from the previous Office action and maintained for reasons of record. Applicants' argument is not persuasive for reasons set forth above.

Claim Rejections-35 USC § 112

7. The following is a quotation of the **first** paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 67-68, 70-71, and 73-74 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to nucleic acid molecules comprising the sequence of SEQ ID NO:635 or 100 contiguous nucleotides thereof, or vector comprising the nucleic acid molecules and recombinant cell comprising such vector.

The claims are rejected mostly for the same reasons as those set forth in the "Revised Interim Written Description Guidelines Training Material" for similar claim limitations. The training material is available on the US PTO's website: http://www.uspto.gov/web/patents/guides.htm, and its relevant sections are attached to this Office action. Please especially see Examples 7, 9-11, and 14.

For example, in regard to claim 67 and its dependent claims, and claim 74, see example 7 because SEQ ID NO:635 is only a fragment of a full-length open reading frame. Due to the use of "comprising" and the fact that SEQ ID NO:635 is only part of an open reading frame, the claimed nucleic acids read on full-length ORF which is yet to be discovered.

Take as a specific example of claim 68 as to the limitation "hybridizes under stringent condition". The claim is drawn to a genus of polynucleotides including any

nucleic acids that hybridize to nucleic acids comprising SEQ ID NO:635, or a 100mer thereof. Since the claim does not specify any particular stringency conditions (low, medium or high) for the hybridizations, and do not contain functional limitations, the claim is broad and read on a variety of nucleic acids. Clearly, there is substantial variability among the species encompassed by the scope of the claims because the genus encompasses a variety of species with different structures and distinct functions. While the specification gives an example of the "stringent condition" as 50°C (see page 3), absent a clear definition in the specification, the term is broad and can be including temperatures lower than 50°C. A description of a genus may be achieved by means of a recitation of a representative number of species, falling within the scope of the genus, or by means of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly & Co., 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In the instant case, the specification discloses only a species: the nucleotide sequence of SEQ ID NO:635, but, as set forth above, the lack of a clear stringency of hybridization conditions and the lack of functional limitation in the claims would be expected to yield structurally unrelated nucleic acid molecules. Thus, the single disclosed species is not representative of the genus because there is no structural attribute or feature that is common to the members of the genus.

Applicant's arguments filed 10/16/03 have been fully considered but they are not persuasive.

Applicants argument is on the ground that while it is agreed that the claimed polynucleotides read on full-length ORF, which is not disclosed in the specification, not

all species in the claimed genus need to disclosed. This is not persuasive because while applicants do not need to disclose all the species, a representative number of species, or a distinguishing characteristics for the species need to be disclosed. In the instant case, applicants only disclosed the sequence of SEQ ID NO:635, and no distinguishing characteristics for all the species encompassed by the claimed genus are disclosed. Thus, one skilled in the relevant art would have reasonable doubt that the inventor(s), at the time the application was filed, had possession of the claimed invention.

9. The rejections of claims 67-68, 70-71, and 73-74 under 35 U.S.C. 112 , second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is hereby withdrawn in view of the amendments to the claims.

10. The rejection of Claims 67-68, 70-71, and 73-74 under 35 U.S.C. § 102(b) as being anticipated by Hillier et al. (GenBank accession No. R87679.1, 8/16/1995) is hereby withdrawn in view of the amendments to the claims.

11. The rejection of Claims 67-68, 70-71, and 73-74 under 35 U.S.C. § 102(b) as being anticipated by Lin et al. (US patent No. 5,712,381, Date of Patent: Jan. 27, 1998, Date of Filing: Aug. 15, 1996) is hereby withdrawn in view of the amendments to the claims.

Conclusion

12. No claim is allowed.

13. THIS ACTION IS MADE FINAL.

14. Applicants are reminded of the extension of time policy as set forth in 37 C.F.R. §1.136 (a). A shortened statutory period for response to this final action is set to expire three months from the date of this action. In the event a first response is filed within two months of the mailing date of this final action and the advisory action is not mailed until after the end of the three-month shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. §1.136 (a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than six months from the mailing date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shubo (Joe) Zhou, whose telephone number is 571-272-0724. The examiner can normally be reached Monday-Friday from 8 A.M. to 4 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on 571-272-0722. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst Tina Plunkett whose phone number is (571) 272-0549.

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Shubo (Joe) Zhou, Ph.D.

Patent Examiner

JOHN S. BRUSCA, PH.D
PRIMARY EXAMINER